

***Remarks***

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1-109 and 111-116 in condition for allowance or materially reducing the number of issues for appeal. Applicants submit that the proposed amendments of claims 22, 48, 85, 93, 94, 101, 102, 104, and 107-109, and proposed new claims 113-116 do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined.

Upon entry of the foregoing amendment, claims 1-109 and 111-116 are pending in the application, with claims 5, 48, 61, 85, 93, 95, and 97 being the independent claims. Claims 22, 48, 85, 93, 94, 101, 102, 104, and 107-109 are sought to be amended, new claims 113-116 are sought to be added, and claim 110 is sought to be canceled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested. Applicants assert the right to file one or more divisional applications for the subject-matter canceled.

Support for the amendments can be found in the original specification and claims as originally filed. Specifically, support for the new claims 113-116 can be found, *inter alia*, in claims 15, 16, 20, and 21 as originally filed.

Claim 22 has been amended by canceling the phrase "Q is N and" as redundant.

Claims 48 and 93 have been amended by limiting the definition for "Q" to N. Further, the phrase "D is Q or a bond" has been replaced in claims 48 and 93 with --D is O, S, or a bond--. A similar amendment has been made in claim 85. Applicants submit that

no new matter has been introduced by these amendments since deletion of individual members of a Markush expression does not constitute new matter. *See, In re Johnson and Farnham*, 194 USPQ 187 (CCPA 1977).

Claim 93 has been amended by replacing the definition "an alkylene or an alkylene ether" for R<sub>7</sub> and R<sub>8</sub> with the correct definition --H or a carbohydrate--. Support for this amendment can be found, *inter alia*, in claims 11, 12, 13, 20, 21, 23, 25, 27, 32, 33, 35, 37, 39, 41, 51, 58, 66, 68, 73, 75, 80, and 82.

Claim 94 has been amended by excluding the dependency from the canceled claim 110. Claims 101, 102, 104, and 107-109 have been amended to be dependent on claim 5 instead of the canceled claim 110.

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejection under 37 C.F.R. § 112, first paragraph***

The Examiner has rejected claims 1-9, 11, 15, 20, 21, 29, 42, 45, 48, 63, 70, 77, 93, and 94-110 under 35 U.S.C. § 112, first paragraph, for reasons already made of record and notwithstanding Applicants' traverse. The Examiner alleges that claims 1-9, 11, 15, 20, 21, 29, 42, 45, 48, 63, 70, 77, 93, and 94-110 are non-enabled. Applicants respectfully traverse this rejection. However, solely to expedite the prosecution of the pending claims,

Applicants have canceled claim 110 and amended claims 48 and 93 by limiting the scope to amine derivatives, i.e., to compounds where the Q<sup>+</sup> moiety is N (nitrogen).

Applicants again note that claims 5-9, 29, 42, and 95-100 on file are already directed to amine derivatives, i.e., to compounds where Q<sup>+</sup> is N. Thus, based on the Examiner's arguments, Applicants assume the Examiner has inadvertently rejected claims 5-9, 29, 42, and 95-100 under 35 U.S.C. § 112, first paragraph, and request that the rejection be withdrawn.

In view of the above, reconsideration and withdrawal of the rejection of claims 1-9, 11, 15, 20, 21, 29, 42, 45, 48, 63, 70, 77, 93, and 94-110 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

### ***Objections***

The Examiner has objected to claims 10, 12-14, 16-19, 22-28, 43-44, 46-47, 49-62, 64-69, 71-76, 78-92, and 111-112 as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

In view of the above amendments, Applicants believe the objection has been rendered moot. Accordingly, reconsideration and withdrawal of the objection to claims 10, 12-14, 16-19, 22-28, 43-44, 46-47, 49-62, 64-69, 71-76, 78-92, and 111-112 are respectfully requested.

### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn.

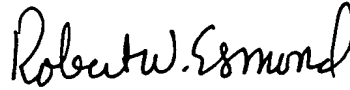
Further, Applicants submit that the entry of the amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims. In view of the foregoing remarks, Applicants submit that the claimed invention, as amended, is neither anticipated nor rendered obvious in view of the prior art reference cited against this application. Applicants therefore request the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

It is believed that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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**Version with markings to show changes made**

***In the Claims:***

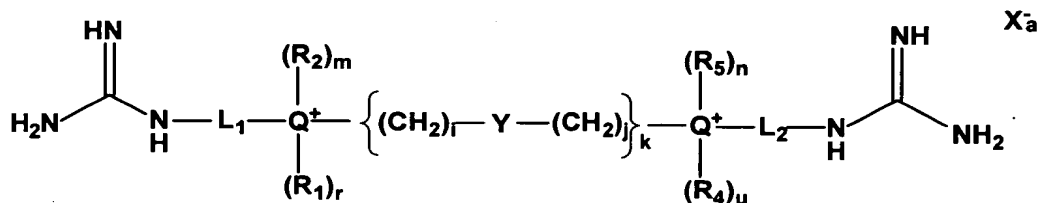
Claim 110 has been canceled.

New claims 113-116 have been added.

Claims 22, 48, 85, 93, 94, 101, 102, 104, and 107-109 have been amended as follows:

22. (Once amended) The compound as claimed in claim 21, wherein [Q is N and] R<sub>7</sub> and R<sub>8</sub> are H.

48. (Twice amended) A compound having the formula:



wherein

Q is [selected from the group consisting of] N[, O, and S];

R<sub>1</sub> and R<sub>4</sub>, independently of one another, are selected from the group consisting of H, -(CH<sub>2</sub>)<sub>p</sub>-D-Z, an alkyl, an alkenyl, an alkynyl, an aryl, and alkyl ether, wherein any of R<sub>1</sub> and R<sub>4</sub> are optionally substituted by one or more of an alcohol, an aminoalcohol, an amine, an amide, an ether, a polyether, a polyamide, an ester, a mercaptan, an alkylthio, a urea, a thiourea, a guanidyl, or a carbamoyl group, and wherein at least one of R<sub>1</sub> and R<sub>4</sub> is a straight chain or branched, cyclic, alkenyl, alkynyl or aryl group having from about 6 to about 64 carbon atoms;

D is [Q] O, S, or a bond;

p is an integer from 0 to about 100;

Z is selected from the group consisting of amine, spermyl, carboxyspermyl, guanidyl, spermidinyl, putricinyl, diaminoalkyl, pyridyl, piperidinyl, pyrrolidinyl, polyamine, amino acid, peptide, and protein;

m, n, r, and u are 0 or 1;

R<sub>2</sub> and R<sub>5</sub>, independently of one another, are selected from the group consisting of H and a C<sub>1</sub> - C<sub>8</sub> alkyl, alkenyl, aryl, and alkyl optionally substituted by one or more of an

alcohol, an amine, an amide, an ether, a polyether, a polyamide, an ester, a mercaptan, a urea, a thiourea, a guanidyl, or a carbamoyl group;

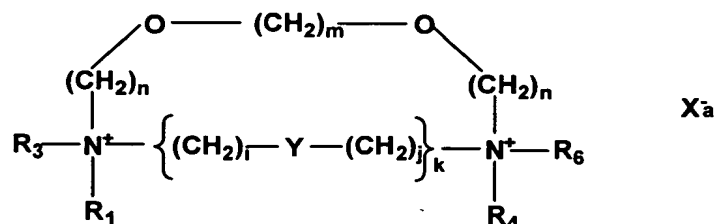
i and j are integers from about 2 to about 3;

k is an integer from 1 to about 3;

$L_1$  and  $L_2$ , independently from one another, are an alkylene or an alkylene ether; and

Y is selected from the group consisting of  $CH_2$ , O, S and NH.

85. (Twice amended) A compound having the formula:



wherein

Y is selected from the group consisting of  $CH_2$ , an ether, a polyether, an amide, a polyamide, an ester, a sulfide, a urea, a thiourea, a guanidyl, a carbamoyl, a carbonate, a phosphate, a sulfate, a sulfoxide, an imine, a carbonyl, and a secondary amino group and wherein Y is optionally substituted by  $-X_1-L'-X_2-Z$  or  $-Z$ ;

$R_1$ ,  $R_3$ ,  $R_4$  and  $R_6$ , independently of one another, are selected from the group consisting of H,  $-(CH_2)_p-D-Z$ , an alkyl, an alkenyl, an alkynyl, an aryl, and an alkyl ether, wherein any one of  $R_1$ ,  $R_3$ ,  $R_4$ , and  $R_6$  are optionally substituted by one or more of an alcohol, an aminoalcohol, an amine, an amide, an ether, a polyether, a polyamide, an ester, a mercaptan, an alkylthio, a urea, a thiourea, a guanidyl, or a carbamoyl group, and at least one of  $R_1$ ,  $R_3$ ,  $R_4$  and  $R_6$  is a straight chain or branched, cyclic, alkyl, alkenyl, alkynyl or aryl group having from 6 to about 64 carbon atoms; and  $R_1$ ,  $R_3$ ,  $R_4$  and  $R_6$  may optionally be covalently linked with each other or with Y, to form a cyclic moiety;

Z is selected from the group consisting of amine, spermyl, carboxyspermyl, guanidyl, spermidinyl, putricinyl, diaminoalkyl, pyridyl, piperidinyl, pyrrolidinyl, polyamine, amino acid, peptide, and protein;

$X_1$  and  $X_2$ , independently of one another, are selected from the group consisting of NH, O, S, alkylene, and arylene;

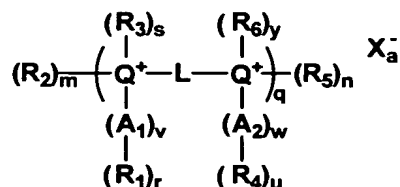
$L'$  is selected from the group consisting of alkylene, alkenylene, alkynylene, arylene, alkylene ether, and polyether;

D is [Q] O, S, or a bond;

m and n are 0 or 1; and

i, j, k, l and p are integers from 1 to about 10.

93. (Twice amended) A compound having the formula:



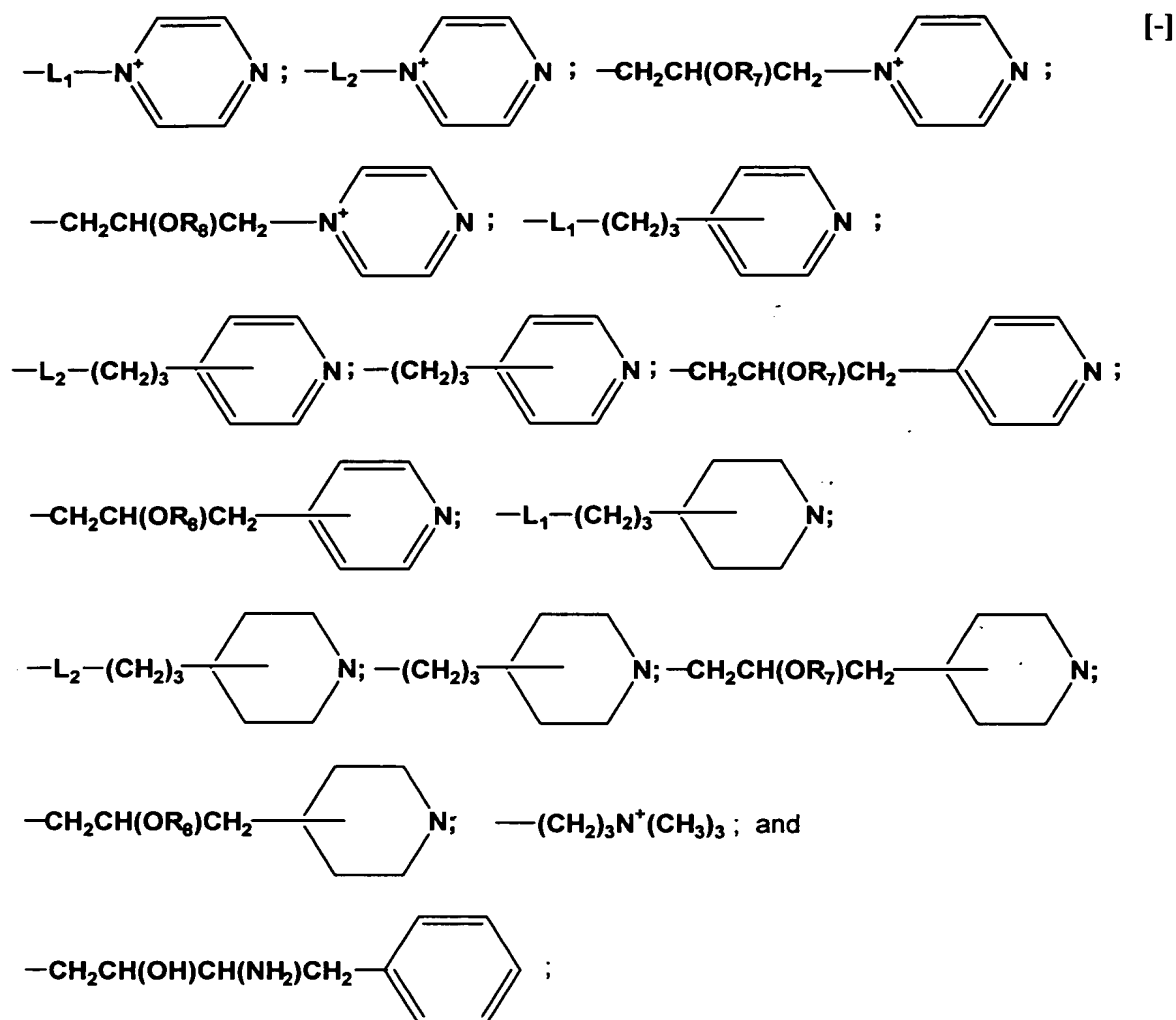
wherein

Q is [selected from the group consisting of] N[, O and S];

L is a bivalent organic radical capable of covalently linking each Q;

$R_1 - R_6$ , independently of one another, are selected from the group consisting of H,  $-(CH_2)_p-D-Z$ , an alkyl, an alkenyl, an alkynyl, an aryl, and alkyl ether, wherein any one of  $R_1-R_6$  are optionally substituted by one or more of an alcohol, an aminoalcohol, an amine, an amide, an ether, a polyether, a polyamide, an ester, a mercaptan, an alkylthio, a urea, a thiourea, a guanidyl, or a carbamoyl group, and wherein at least one of  $R_1$ ,  $R_3$ ,  $R_4$  and  $R_6$  is a straight chain or branched, cyclic, alkyl, alkenyl, alkynyl or aryl group having from about 6 to about 64 carbon atoms and at least one of  $R_2$ ,  $R_3$ ,  $R_5$  and  $R_6$  is selected from the group consisting of  $-CH_2CH(OR_7)CH_2NH_2$ ;  $-CH_2CH(OR_8)CH_2NH_2$ ;  $-(CH_2)_bNHC(O)Z$ ;  $-(CH_2)_cNHC(O)Z$ ;  $-CH_2CH(OR_7)CH_2NHC(O)Z$ ;  $-CH_2CH(OR_8)CH_2NHC(O)Z$ ;  $-CH_2CH(OR_7)CH_2NHC(NH)NH_2$ ;  $-CH_2CH(OR_8)CH_2NHC(NH)NH_2$ ;  $-L_1-N(CH_2CH_2OH)_2$ ;  $-L_2-N(CH_2CH_2OH)_2$ ;  $-(CH_2)_4N[-(CH_2)_8-CH=CH-(CH_2)_7-CH_3]-CH_2-CH(OR_7)CH_2NH_2$ ;  $-(CH_2)_4N[-(CH_2)_8-CH=CH-(CH_2)_7-CH_3]-CH_2-CH(OR_8)CH_2NH_2$ ;





and  $R_1$  and  $R_4$  or  $R_3$  and  $R_6$  may optionally be covalently linked with each other, or with L to form a cyclic moiety;

Z is selected from the group consisting of amine, spermyl, carboxyspermyl, guanidyl, spermidinyl, putricinyl, diaminoalkyl, pyridyl, piperidinyl, pyrrolidinyl, polyamine, amino acid, peptide, and protein;

D is [Q] O, S, or a bond;

$A_1$  and  $A_2$ , independently of one another, are selected from the group consisting of  $CH_2O$ ,  $CH_2S$ ,  $CH_2NH$ ,  $C(O)$ ,  $C(NH)$ ,  $C(S)$  and  $(CH_2)_i$ ;

X is a physiologically acceptable anion;

$L_1$  and  $L_2$ , independently from one another, are an alkylene or an alkylene ether;

$R_7$  and  $R_8$ , independently from one another, are [an alkylene or an alkylene ether] H or a carbohydrate;

b and c are integers independently selected from 1 to about 4;

m, n, r, s, u, v, w and y are 0 or 1, with the proviso that when both m and n are 0 at least one of r, s, u and y is other than 0;

p and t are integers from 0 to about 100;  
q is an integer from 1 to about 1000; and  
a is the number of positive charge divided by the valence of the anion.

94. (Three times amended) The compound as claimed in any one of claims 1, 5, 48, 85, 89, and 93, [and 110] wherein said cyclic group is a cholesteryl group.

101. (Three times amended) A composition comprising one or more compounds of any one of claims 1, 5, 37, 38, 48, 61, 85, 93, 95, and 97[, and 110].

102. (Three times amended) A composition comprising one or more compounds of any one of claims 1, 5, 37, 38, 48, 61, 85, 93, 95, and 97[, and 110] and at least one additional component selected from the group consisting of a cell, cells, a cell culture, a cell culture media, a neutral lipid, a nucleic acid, and a transfection enhancer.

104. (Three times amended) A lipid aggregate comprising one or more compounds of any one of claims 1, 5, 37, 38, 48, 61, 85, 93, 95, and 97[, and 110].

107. (Three times amended) A kit comprising one or more compounds of any one of claims 1, 5, 37, 38, 48, 61, 85, 93, 95, and 97[, and 110] and at least one additional component selected from the group consisting of a cell, cells, a cell culture media, a nucleic acid, a transfection enhancer and instructions for transfecting a cell or cells.

108. (Three times amended) A method for introducing a polyanion into a cell or cells, said method comprising forming a liposome from a positively charged compound of any one of claims 1, 5, 37, 38, 48, 61, 85, 93, 95, and 97[, and 110], contacting the liposome with a polyanion to form a positively-charged polyanion-liposome complex and incubating the complex with a cell or cells.

109. (Three times amended) A method for introducing a biologically active substance into a cell, said method comprising forming a liposome of a compound of any one of claims 1, 5, 37, 38, 48, 61, 85, 93, 95, and 97[, and 110] and a biologically active substance and incubating the liposome with a cell or cell culture.